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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,411	03/09/2004	Chih-Ming Chen	300.1005 CON	9033

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EXAMINER	
YOUNG, MICAH PAUL	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 08/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/796,411	CHEN ET AL.	
	Examiner	Art Unit	
	Micah-Paul Young	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20 and 28-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 28-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 4/17/06
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment of Papers Received: Amendment/Response dated 3/31/06 and 5/15/06.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 1-20 and 28-30 rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Whitcomb (USPN 6,011,049 hereafter '049) and Byrd et al (USPN 6,191,162 hereafter '162). The claims are drawn to controlled release formulation comprising metformin where the dosage forms comprises a core and membrane coating. The core and coating comprise common excipients well known in the art such as binders and plasticizers.

4. The '049 patent teaches a once-a-day oral metformin formulation for the treatment of diabetes mellitus (abstract, col. 5, lin. 7-24). The formulation comprises control-release carriers such as starch, gelatin and methylcellulose and takes the form of tablets or capsules (col. 5, lin. 27-33). The formulations comprise from 300 – 2000 mg of metformin (claims). The disclosure is silent to the particular AUC values however the concentrations of the metformin are identical to those of the instant claims. It is the position of the Examiner that the formulations of the '049 would inherently possess these properties since the concentrations are identical and applicant has not provided any other defining features of the claims. The '049 patent discloses a metformin

formulation comprising common excipients in tablet or capsule form, however the disclosure is silent to a specific core or coating structure. This is however well known in the art and would be obvious to one of ordinary skill. This can be seen in the '162 patent.

5. The '162 patent teaches a controlled release formulation capable of reducing serum glucose levels (abstract). The formulation comprises multiple pharmaceuticals including biguanides such as metformin (col. 8, lin. 23-61). The cores include excipients like binders and absorption enhancers such as polyvinylpyrrolidone and fatty acid esters (mono-, di-, and triglycerides (col. 18, lin. 30-37, lin. 55-60). The coating includes alkycelluloses, and other common hydrophobic coatings such as cellulose acetate phthalate (col. 12, lin. 57-65). The coating can also be micro-porous allowing for small amounts of the drug to be released (col. 16, lin. 35-68). The coatings include plasticizers common in the art such as polyethylene glycol and propylene glycol (col. 19, lin. 27-42). The dosages forms include multi-, or single unit granules (col. 12, lin. 39-56). The formulation can be pressed in to min-tablets and filled into capsules (col. 17, lin. 9-32). These coatings and excipient would all have been obvious to the artisan of ordinary skill and would have motivated them to use the excipients in order to tailor the release of the active agent.

6. Regarding the mean serum concentration values, it is the position of the Examiner that these values do not impart patentability barring a showing of an unexpected result. The prior art presents controlled release oral dosage forms that reduce the serum glucose levels in human patients with NIDDM, comprising a dosage of metformin along with a control releasing membrane. The dosage from of Byrd comprises micro-pores that act as passageways for the drug to pass through. The combination of the drug of Whitcomb and the structure of Byrd would

result in a formulation that lowered the serum glucose level in a patient with NIDDM. Burden is shifted to applicant to provide evidence of a patentable distinction in the form of an unexpected result regarding the mean plasma concentration.

7. With these things in mind it would have been obvious to one of ordinary skill in the art to combine the coatings and other excipients of the '162 patent with the formulation of the '042 in order to better control the release of the metformin. It would have been obvious to combine the teachings with an expected result of an improved controlled release formulation capable of treating diabetes mellitus and lowering the serum blood glucose levels in a patient in need thereof.

Response to Arguments

8. Applicant's arguments filed 3/13/06 and 5/15/06 have been fully considered but they are not persuasive. Applicant argues that:

a. The Whitcomb reference does not teach or suggest a formulation suitable for once-a-day dosage, which provides a particular plasma concentration.

b. The Whitcomb does not disclose how the "controlled release dosages forms" are made.

c. The Byrd reference does not suggest the administration of antihyperglycemic drugs.

9. Regarding argument a., it is the position of the Examiner that the "once-a-day" limitations are not to be given patentable weight in a composition claim since they denote methods of use and do not limit the physical components of the dosage from in any way. The dosage forms of the instant claims further need only be suitable for "once-a-day" delivery and

need not themselves actually be "once-a-day" dosages. Any dosage taken all at once can be considered "once-a-day" even if it comprises several tablets, pellets or pills. This "once-a-day" limitation renders the composition claims to a product-by-process interpretation where the process limitations are not given patentable weight. Regarding the teachings of the '049 patent, metformin is delivered in dosages as high as 2000 mg per day and can be delivered up to twice daily, meaning they are capable (the only requirements of the claims) for single daily dosage. Regarding the Tmax concentrations, since the dosage forms of the instant claims must only be suitable to produce such concentrations it I the position of the Examiner that the '049 dosage forms meet this limitations as well. The '049 dosage forms are controlled release oral dosages of metformin, the specific antihyperglycemic of the instant claims. This meets the limitations of the claims. Through routine experimentation by those of ordinary skill in the art, the dosage forms would be suitable and capable of any Tmax concentrations. For these reason the limitations do not impart patentability. For these reasons at least the claims remain anticipated and obviated by the prior art.

10. Regarding argument b., that the '049 patent does not disclose any methods of manufacture, it is the position of the Examiner that such arguments are spurious at best. The claims are drawn to compositions, and not methods of manufacture. As discussed above the disclosures of common excipients, and controlled release dosage forms is seen by the Examiner as sufficient disclosures of a controlled-release dosage form. With these things in mind, the disclosures of the '862 patent sufficiently obviates the claims.

11. Regarding argument c., it is the position for the Examiner that the secondary reference is sufficient to meet the limitations of the claims and does not teach away. The passage cited by

applicant (col. 8, lin. 40-45) states that it is advisable to administer lipoic acid of the invention ***with*** metformin dosage forms. The passage teaches toward co-administration. The claims are drawn using comprising language and open to the inclusion of further pharmaceuticals. Further Byrd is a secondary reference used to establish the level so skill in the art regarding the core and coating structure of metformin dosage forms. The specific structure is well known in the art and is shown by the Byrd reference. One of ordinary skill would be motivated to organize the structure of the '049 into the core, coating structure of Byrd in order to impart structural stability and a controlled release. For these reasons at least the claims remains obviated.

Conclusion

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 571-272-0608. The examiner can normally be reached on M-F 7:00-4:30 every other Monday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Micah-Paul Young
Examiner
Art Unit 1618

MP Young

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER